THE BLOOD SEDIMENTATION RATE IN TUBERCULOSIS:

A Study of 148 Patients.

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A Thesis for the Degree of Doctor of Medicine

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The Blood Sedimentation Rate in Tuberculosis.

A Study of 148 Cases.

The beginnings of this test, at first acclaimed by some writers as a diagnostic test for tuberculosis, and with increasing investigation gradually relegated to the evergrowing group of non-specific reactions, go very far back in the history of medicine. Galen noted the presence of a layer of fluid above coagulating drawn blood, and throughout the era of blood letting as a therapeutic measure, physicians frequently referred to this crusta sanguinis which formed and remained above the coagulum.[1] Thomas Sydenham remarked its appearance in several diseases, such as smallpox, pleurisy and rheumatic fever, which, though clinically far apart, had two common characteristics in raised temperature and the presence of this crusta sanguinis in drawn blood. It was only natural therefore, that, attracting attention as it did throughout the earlier days of medicine, the crusta sanguinis, size, or buffy coat, should have been looked on as intimately connected with the cause and nature of disease. Lovatt Evans[2] in "Recent Advances in Physiology" writes: "If we except the facts of the circulation of the blood, it may be questioned whether any phenomenon within the purview of medical/

medical knowledge has in the past had such a profound influence on its practices as has this simple fact of the occurrence of the buffy coat, for it represents the basal observation on which rested the theories of humoral pathology from the time of Hippocrates up till the middle of last century." This humoral theory was eventually replaced by the cellular theory of Virchow, but up till then it remained supreme; and the buffy coat was practically forgotten to attract attention again only quite recently.

The nature and causation of this crusta sanguinis, size, or buffy coat evidently aroused considerable interest among physicians as far back as the 18th century. (3) Hewson showed that it was as definitely part of the whole blood as were the corpuscles and was the first to demonstrate that the change was due to a more rapid rate of fall of the corpuscular elements; noting also the fact that blood giving the reaction was as a rule slower to coagulate than was normal blood. His work also showed that the change in the blood lay really in the plasma since separated corpuscles from normal blood and from blood which we would now say had a rapid sedimentation rate, fell at equal rates if suspended in the same medium. (4) In the early 19th century Scudamore showed that increased rate of fall was associated with increased/

increased blood fibrin and later Nasse[5] while confirming Scudamore's observations showed the presence of two additional factors. He noted the tendency to cluster of the red cells and also showed that after exclusion of blood fibrin as a factor by defibrination, such corpuscles still fell more rapidly in buffy blood than in normal. Pfeifer[6] in the last few years of the 19th century showed that the increased rate of fall was not due to increased viscosity.

In more recent times considerable work has been done and published by Fahraeus[7], along with a comprehensive history of the reaction. He confirmed the observations made by Hewson that differences in the specific gravity of plasma and cells had little to do with the rate of fall. He also showed the accuracy of Nasse's work which as mentioned above noted the presence of agglutination, the increase of blood fibrin and the existence of still another factor. This factor Fahraeus showed to be the presence of increased blood globulin. Red cells were found hardly to sediment at all in a solution of pure albumen, while in a solution of fibrinogen they fell rapidly. If suspended in a solution of globulin, the rate of fall was intermediate to the last two. The nature of the blood proteins seems to be intimately connected, therefore, with the sedimentation rate, or, as Fahraeus prefers it the suspension stability of the blood, and since increase of blood globulin seems to cause haem-

agglutination the whole seems a reasonable hypothesis to explain increase or decrease in the rate of the falling corpuscles. Confirmation is obtained on finding that by increasing the serum globulin the sedimentation rate is increased. Thus it has been shown that if the corpuscles of citrated blood be removed from the serum and the serum exposed in a quartz tube to ultra-violet rays, the reconstitution of the blood by addition of its corpuscles leads to a marked increase in the rate of fall of the red cells. This is due to the action of the ultra-violet rays in converting serum albumen into serum globulin, and if the exposure is made in a glass tube which does not transmit the actinic end of the spectrum, no such conversion takes place and no increase in rate of fall is noted.

It is therefore reasonable to expect increased sedimentation rate in those conditions in which increase of blood fibrinogen or globulin is found. Such increase is known to occur in pregnancy and several workers have noted an increased sedimentation rate during gestation. (8) Blundell in a lecture delivered in 1828 said: When women are pregnant the blood is more or less sizy ..... in conjunction with other signs it is a valuable indication of pregnancy..... According to Fahraeus the sedimentation rate is increased in/

in all acute infections, most distinct when accompanied by high fever, and according to Halliburton, quoted by Fahraeus, the serum globulin is definitely increased in such conditions and reaches a maximum in pneumonia, diabetes mellitus and parenchymatous nephritis. Beaumont and Dodds (9) hold that increased tissue destruction causes raising of the blood fibrinogen and globulin and on this fact chiefly rests the importance of the test in tuberculosis and in malignant disease. Fahraeus himself thought that an increased sedimentation rate was a beneficial reaction of the body to infection or other change. He says "if we suppose the globulin increase during pregnancy and in disease, play, in point of principle, the same role, then the presence of this change in pregnancy speaks against interpreting the change as a pathological derangement". In addition he remarks the fact that antitoxin is usually closely bound up with the globulin fraction of the blood proteins and suggests that there may be antibody increase pari passu with increasing blood globulin. In malignant disease at least and in tuberculosis to a lesser extent, such views seem hardly tenable and the view usually accepted is that an increased blood sedimentation rate is symbolic of increased cell destruction.

As has been said before the whole hypothesis and its application to tuberculosis seems reasonable. Other

explanations for the behaviour of the red cells have been put forward. Recently Pinner Knowlton and Kelly (10) have investigated the relationship between increased blood fibrinogen and cholesterol and an increased sedimentation rate. Tney can, however, find little or no correspondence between either the first two and the last. Their publication is one of several in recent years in which the test is reported as quite unreliable as an index of cell destruction. Other explanations such as increase of platelets, alterations in surface tension, change in the electrical charges of the blood elements and the volume of red cells have all been put forward. Anaemia of itself need not be associated with increased blood sedimentation rate and one writer reports a case of very intense anaemia in which the rate was normal.

It was accordingly as a gauge of tissue destruction that the test was first applied to tuberculosis, and for some time it was thought that an idea of the activity of any case might be obtained by finding the blood sedimentation rate. Since its introduction into sanatorium practice by Westergren (11) a very considerable literature has accumulated, and at first considerable importance was attached to the readings. More recently articles written on the subject have shown a less definite bent, and most writers content themselves with

concluding that, taken in conjunction with the more or less established methods of assessing activity, the test may prove of some use. A few remain enthusiastic and maintain that in tuberculosis it is of greater value than the temperature or the pulse, and an equal number in more recent times condemn the reaction as useless if not misleading. The material presenting itself it seemed a profitable line of research to the writer to investigate the matter for himself. The tests done were done wholly from the tuberculosis point of view, except in so far as any case or group of cases, reading or series of readings, seemed to have any direct bearing on the pathology of the reaction.

Before discussing the various methods of performing the reaction the writer proposes to discuss briefly the broad features of the clinical material utilised. 77 cases were pulmonary and 71 cases were non-pulmonary. Several pulmonary cases were complicated by laryngitis, and a number by the so-called surgical tuberculous lesions. In the particular resume on the pulmonary patients this question of complications will be more fully discussed. Among the patients with non-pulmonary lesions by far the greatest number suffered from bone and joint infection. There were also a few instances of glandular and skin disease, abdominal/

abdominal tuberculosis and renal phthisis in its various stages. It was chiefly in these surgical lesions that the writer was interested. In these the generally recognised constitutional signs of a tuberculous infection may be singularly latent. Temperature rises are present in almost all patients when first seen and the pulse rate may be abnormally rapid. These signs however should, within a short time of the commencement of efficient treatment, be scarcely recognisable, and on an average the general nutrition of the patient is better than in a phthisical patient showing comparable temperature and pulse changes. It has been the writer's experience that when an apparently uncomplicated case of tuberculosis of bone or joint displays, after one or two months treatment any of the changes associated with the more generalised effects of tuberculosis, such changes are due to the existence of some hitherto unsuspected pulmonary lesion and less often to tuberculous abdominal glands. In the tables and figures which follow such instances will be specifically mentioned. Fortunately such cases are not the rule, at least so far as concerns activity of the complicating lesion; Fraser (12) however maintains that foci in bronchial or abdominal glands are the antecedent lesions in most cases of bone or joint tuberculosis and/

and to this opinion the writer subscribes. Accordingly the clinician is faced with a type of patient who does not as a rule show general signs of activity for any great length of time. Locally it is recognised that activity persists for a much longer period and while this activity can be assessed in various ways, most of which involve movement and manipulation, it seemed reasonable to investigate the question as to whether or not an idea of the activity of a lesion could be arrived at by finding the patients' blood sedimentation rate. On a similar line of reasoning the test was applied to obviously active cases to see whether or not it foreshadowed abscess formation or the deposit elsewhere of bacilli. The test was therefore done at regular intervals of six weeks in both pulmonary and non-pulmonary groups and in both the occurrence of any event in a patient's progress was taken as an indication for an additional reading, confirmatory or interrogatory, as the case might be.

The test in its essentials consists in finding how quickly the blood cells fall in a mixture of blood and some anticoagulant solution in proportions which vary slightly with the method employed. Fahraeus' original method is as follows; a vein is entered and the blood run

directly/

directly into 2 ccs of 2% sodium citrate solution. This is contained in a tube 17 cm. long and 9 mm. bore, with a mark at its upper end to denote a content of 10 ccs. To this mark the blood is allowed to fill and blood and citrate mixed by inversion. After standing vertically for one hour the reading is expressed as a depth of clear fluid above the sedimented cells. In Linzemeir's[13] method, the tube has a cubic content of one cubic centimetre and is 6.5 cm. high and 3 to 4 mm. in diameter. At the level of one cc. there is a mark up to which the blood and citrate mixture reaches and below this marks 6, 12 and 18 mm. from it. A 1 cc. syringe containing .2 cc of 5% citrate solution is used both to collect and mix the blood and citrate, and after .8 ccs. of blood have been drawn in mixing takes place by sucking in a bubble of air and further movement. In this method readings are expressed as the time the sedimenting cells take to reach the successive marks, though commonly the time taken to reach the lowest or 18 mm. mark is the most useful reading. According to its originator this method gives a reading of 250 to 300 minutes for normal blood to reach the lowest mark. Westergren's[14] method is a modification of Fahraeus' technique. The proportion of blood and citrate, which is 3.8% strength, remains as for the/

the two previous i.e. 4 to 1. The mixture of this proportion is got by means of a special syringe and after withdrawal from the vein, intimate mixing is got by inversion in a 2 cc. test tube. The actual test is done in a tube 30 cm. long and 2.5 mm. internal diameter, closed at the lower end and having a mark 200 mm. from that end. When the blood-citrate mixture is sucked up to this mark the contents are approximately 1 cc. The finding is expressed as a depth in millimetres of clear fluid at the end of one and of two hours, the tube standing vertically throughout. The method adopted by Zeckwer and Goodall resembles that of Linzemeir. A 15 cc. centrifuge tube graduated in tenths of a cc. is used and 3% sodium citrate is the chosen anti-coagulant. Blood is run directly from a vein into the tube in which are 2 ccs. of the citrate solution and mixing is by inversion. The tube is left upright and the reading taken after one hour. Here, however, it is expressed as the volume of cells which have sedimented in that time and for normal blood a reading of 7.1 ccs. in one hour is to be expected. Morriss (15) has slightly adapted the Westergren technique. Using 3.8% sodium citrate a mixture of the usual proportions is made and proper mixing done in an ordinary Wasserman tube. Thereafter a 1 cc. pippette is filled from the mixture and placed vertically. As the pippette is marked off in 100 divisions the result is

easily/

easily expressed as a percentage. Normally men give a reading of 1-5% and women 5-10% by this method. Other modifications of the Westergren technique include Trail's,[16] Heaf's[17] and Cummin's.[18]

It is therefore seen that several methods are available, and the result may be expressed in different ways. A reading may be expressed as a volume of cells or as a volume of clear supernatant fluid in a given time or either one or the other may be expressed as a percentage of the whole. Alternatively to these methods as a group the sedimentation element may be stabilised and the time factor used as the variable. This takes place in Linzemeir's method and its modifications where the reading is the time in minutes taken by the upper level of cells to reach a fixed mark or series of marks. In America and the Scandinavian States the method of preference seems to be Westergren's or Morriss's adaptation, while on the continent and chiefly in Germany a considerable body use Linzemeir's technique. In this country there is considerable variety in the methods used but most of the published work seems to have been done on the lines of Westergren's work.

From the tables given later it will be seen that a large number of the patients consisted of children, in whom it can be a matter of considerable difficulty to perform venous/

venous acupuncture. This factor made it desirable that as small a quantity of blood as possible should be necessary and mitigated against the adoption of Zeckwer's and Goodall's method, where 8 ccs. of blood are required. Linzemeir's technique being the simplest, requiring only 1 cc. of blood, was used throughout, and its sole disadvantage seemed to be that a longer time had to elapse before a final reading could be arrived at. As in other methods such as Westergren's and Morriss's a curve of the rate of fall could be plotted if desired, and the tubes being of wider bore than in other methods, the possibility of successive readings being widely divergent through difference in the diameter of the separate tubes on the rack, was minimised. (19) Fitschel has pointed out in the Westergren methods that considerable care must be taken that both in length of the 1 cc. column and in bore, the tubes must be very accurately calibrated. It might be said against Linzemeir's method that wide variations exist in figures for normal blood and many writers report cases taking from 400-900 minutes to reach the lowest mark. Among those using this method these readings are looked on as normal and certainly such a conclusion seems in keeping with the most acceptable explanations of the test. It must be remembered that in Linzemeir's method, as opposed to those in which the time factor is fixed, a rapid sedimentation/

sedimentation rate results in a low reading expressed in minutes (and vice versa).

TECHNIQUE.

The essentials of the apparatus have already been described. One fifth of a cc. of 5% sodium citrate is drawn into a Record Syringe capable of holding rather over 1 cc., graduated in 1/10 cc., and a long fine hypodermic needle attached. This type of needle was preferred as being longer and stronger than the ordinary hypodermic needle, though not causing any greater discomfort due to proportionate increase in bore found in intravenous needles. The skin over the cubital fossa having been cleansed with spirit followed by methylated ether, a vein is entered and the syringe filled with blood up to the 1 cc. mark. If at all possible no ligature should be used to make the vein more prominent, as it is known that the resultant rise in CO_2 tension of the blood causes more rapid sedimentation. The syringe having been withdrawn, a further movement of the plunger causes the indrawing of a bubble of air, and by gently tilting and rotating the syringe this is used to obtain a uniform mixture of blood and citrate. This mixture is then filled into one of the tubes, the needle being kept in position throughout. The length of needle used makes it possible to fill the tube up to the upmost mark/

mark without frothing or accumulation of bubbles, which prior to the adoption of this type of needle, constantly occurred. Their presence was found to interfere with accurate reading when filling and to delay sedimentation quite appreciably. The test tube used is one of a rack of ten, and the patient's name, the number of the tube, and the time of filling are noted. In the modern modifications of the Westergren group of methods, the rack of tubes is then placed in an incubator at 37°C., since it is known that the higher the temperature the more rapid is the rate of fall. Such a procedure is obviously impracticable in Linzemeir's method, but the rack may be placed in a ward annexe of known steady temperature and means taken to keep this as constant as possible.

The use of a rack of ten tubes makes it possible to do ten tests at a session. This can be done accurately and expeditiously by the use of two or three syringes known to correspond closely in cubic capacity with the tubes and with each other, and by having ten suitable needles ready sterilised. It was found that no appreciable disadvantage accrued to keeping syringes and needles in sterile normal saline prior to use, though the method of election would probably be to use these dry. On no account should phenol, spirit or free ether be used in this connection unless it is carefully/

carefully removed by saline prior to taking off the blood, as these by causing haemolysis or coagulation seriously interfere with the rate of reaction. By general attention to the method suggested, the slightest possibility of mixture of incompatible bloods even in minute traces becomes hypothetical. The tubes themselves should be carefully cleaned after each series has been done and dried by passing through alcohol and ether. They should then be kept dry and free from dust until next used.

THE CLINICAL MATERIAL. (A) PULMONARY TUBERCULOSIS.

As previously stated the test was carried out on a series of patients with pulmonary lesions and on a series suffering from conditions variously classified as surgical or non-pulmonary tuberculosis. These latter will be separately dealt with later. In describing the pulmonary group some explanation of the actual facts is necessary. These patients all of them suffered from tuberculosis of the lungs, but apart from the common complications of this disease, a certain number suffered from so-called surgical tuberculous complications. This factor of complications, while offering little or no difficulty in the classification in the administrative sense of such a ward as is suggested, must very properly be taken particular notice of when an attempt/

attempt is being made to correlate the results of a biochemical test with the clinical findings. In the appended table, which shows the grouping of the material at the start of the investigation, consideration was given to the actual state of the surgical complication, and in classifying the cases the actual existence of such a factor as an inactive tuberculous knee or a quiescent consolidated tuberculous spine was not deemed sufficient justification for the insertion of such a case in column C. Such cases were classified in common with the others on the anatomical extent of their pulmonary lesions as in the Turban-Gerhardt scheme, and on the degree of constitutional disturbance irrespective of the mere presence of a complication. This latter factor was expressed by the letters A, B and C and the whole scheme followed thus approximates to that formulated by the Society of Superintendents of Tuberculosis Institutions. (20)

Table 1.

Age	Turban-Gerhardt Classification.												Total
	A1	A2	A3	Total	B1	B2	B3	Total	C1	C2	C3	Total	
-5	–	–	–	–	–	–	–	–	–	–	–	–	–
-10	1	–	–	1	1	–	1	2	–	–	1	1	4
-15	1	1	–	2	1	1	–	2	–	1	1	2	6
-25	–	1	1	2	1	5	1	7	–	2	12	14	23
-35	1	–	1	2	1	–	3	4	–	1	12	13	19
-45	–	–	1	1	–	1	3	4	–	1	3	4	9
45	–	–	–	–	–	–	3	3	–	1	7	8	11
Total	3	2	3	8	4	7	11	22	–	6	36	42	72

Thus/

Thus in all 72 cases were investigated, by far the majority being between the ages of 26 and 35 years. All of these had proven lung lesions, the accepted proof being either radiological or bacteriological, and slightly over 53% of these are to be found in Group C, slightly over 30% in Group B, and a fraction over 11% in Group A. The average case was therefore advanced and clinically fairly ill. Over the whole number 25 suffered from surgical complications. Of these 3 occurred in Column A, but none of those required treatment for their complication, which was in each case quite inactive, and in one was represented by healed scars of very considerable age. In column B, 8 patients had surgical lesions, three of them being quite active and requiring either operative or orthopaedic treatment, and in column C, 14 further such cases were present and only 3 sufficiently inactive as to allow of cessation of active orthopaedic treatment. The 47 remaining cases may therefore be looked on as cases of phthisis. However, as previously stated, there seemed no great objection to including with these, those cases though having surgical complications, were so inactive as not to require active measures. Almost all so added were surgically entirely convalescent, and surgical measures adopted were taken to prevent recrudescence of activity or the assumption of deformity. With these provisos 80% of the charted cases might/

might, for the purposes of the examination, be looked on as cases of pulmonary tuberculosis. It is a noteworthy fact that of the surgically complicated cases with definite surgical activity 78% occur among the advanced and seriously ill cases of column C. Little interest attaches to the commoner complications of phthisis, since almost all such cases occur in Group C, e.g. in all there were 8 cases of laryngitis, only one of which occurred outwith column C. No cases of ischiorectal abscess or sinus occur in either columns A or B.

(A) TESTS DONE: AVERAGE READING.

The total number of readings done was 237 on pulmonary patients. These were done as closely as possible at intervals of 6 weeks. No importance attaches to the average number of readings done per patient since for many reasons some cases could not be pursued over a sufficiently long period. Of the total of 72 cases, 24 had not more than two readings, some having died or been transferred to other institutions and some having left for private reasons. Thirty-four cases were followed over at least 4 readings representing a period of at least 6 months.

For all the cases on Table 1 the average time taken to sediment to the 18 mm. mark was 173 minutes. While the disparity in methods makes it difficult to compare this result mathematically/

mathematically with results obtained by other workers using other methods, it is to be remarked that this reading bears the same ratio to Linzemeir's average normal taken at 275 minutes as Zeckwer's and Goodall's average tuberculosis reading does to their average normal, viz. .6. Similarly if the method of Trail and Stone be transposed into terms of fallen corpuscles and a similar ratio worked out a result of .7 is got.

The average readings for the three groups A, B and C, show a rise from C to A. For C the average works out at 72 minutes, B giving a reading of just over 300 minutes, and A considerably over the same figure. These last two figures are undoubtedly high, but when it is remembered that, as previously mentioned, readings over 300 minutes are well known, and that such are most likely to be found in the cases showing the nearest approach to normal the apparent discrepancy is explained. In addition the general nature of the material resulted in the average for Column A being arrived at from a study of comparatively few cases. No attempt will therefore be made to draw conclusions from these figures. In column C the reading ranged from 190 minutes, which is distinctly above the average reading for all cases, down to about 30 minutes, and the readings for C ii cases were only very slightly higher than those for the Ciii group. The poorest reading was

however/

however higher than that in Column Ciii. In the A and B groups little difference could be found between between 1, 2 and 3 sub groups, all the readings falling into a comparatively short space.

RELATIONSHIP TO ANATOMICAL EXTENT OF DISEASE.

While the argument formulated above regarding the paucity of the cases in group A must be considered, this aspect of the investigation seems to suggest that there is very little relationship between the sedimentation rate and the anatomical extent of the lesion. This in the main is in agreement with the conclusions of Doria (21) and Mathe. (22) Zoekler (23) states definitely that the test is useless as a means of classifying according to the Turban-Gerhardt scheme. Other writers on this subject have referred to the relationship between the sedimentation rate and the degree of lung involvement, but very few have separated this latter factor from the actual nature and present state of the lesion. Luzzato-Fegiz (24) holds that such a relationship does exist, but "is generally related to the anatomical form, extent and activity of the tuberculous process". Some workers have shown a difference in average sedimentation rate between cases chiefly of an exudative type and those chiefly of a productive nature. Among the cases of this investigation 12 might be looked on as almost purely exudative/

exudative and these cases definitely did have very low readings some of them being among the lowest recorded. In the other 60 cases the two processes went on side by side, and radiologically both were represented and recognised. Unfortunately however an assessment of each from an X-ray plate is impossible and sedimentation rate readings from this group touch both the lowest and highest levels attained. Tegtmeier[25] used the sedimentation rate as a means of classifying such cases with the help of radiograms, and associated a rapid fall of corpuscles with the exudative types, and the slower with plates showing a preponderance of cirrhosis. Mathe[22] also arrives at similar conclusions. The few figures available from the present work agree with the findings in the main. While however cases of an almost exudative nature show a rapid sedimentation rate, and cases showing marked cirrhosis tended to approach normal in their sedimentation rate, there remained a large class in which the writer got no more information from the sedimentation rate than from the clinical features of the cases in attempting to assess the preponderance of one process or the other. As will be shown later however the progress of the case, and accordingly the presumable degree of the reparative process is related to the sedimentation rate where a series of readings are taken.

AS/

AS A TEST OF ACTIVITY: (A) GENERAL.

In modern sanatorium practice it matters little whether or not the sedimentation rate of the blood does or does not bear a relationship to the anatomical degree of lung involvement. Such can usually be fairly accurately assessed by ordinary methods of physical examination coupled with radiograms. Nor does it seem reasonable to give too much attention to the nature of the lung processes, apart from the effects thereof on the patient. With few exceptions and excluding complications the state of the patient fairly accurately reflects the swing between exudation, and accordingly spread, and fibrosis, or the defensive reaction of the tissues to a previously laid down exudative lesion. When the exudative type of lesion gains actually, or proportionately through lack of or insufficient reaction to its presence, the patient has very definitely active disease and such activity is manifest to the clinician by signs and symptoms, such as fever, tachycardia, increase of number of bacilli in the sputum, loss of weight, etc. A very cursory study of the average sedimentation rates for A, B and C cases shows that the rate is much lower in those cases which are more ill, and known to be more active. A comparison of the sedimentation rate, therefore, with the various data from which we deduce activity, follows quite logically. According to Westergren (14) a case with an active lesion/

lesion never gives normal valued sedimentation rate and he suggests conversely that with a normal reading an active phthisis can be excluded. Since these statements were made a considerable mass of literature has been added dealing with the same question, and this will be referred to later. The

The question of assessment of activity is one on which probably each clinician has his own favourite standard though admitting and using those commonly accepted. Fishberg (26) states "there is no active phthisis without fever, cough, tachycardia, langor, nightsweats, haemoptysis, etc. Some or all of these symptoms are found soon after the patient becomes actively phthisical". There is definite agreement on most of these points. Sir James Kingston Fowler (27) states that "by observation of the temperature in a case of pulmonary tuberculosis, it is possible to determine the nature of the changes in progress in the lung". Similar definite statements exist as regards the pulse. For an investigation of this sort, however, it seems that the question of activity is indissolubly mixed up with the question of progress; progress after all being the steppage from one degree of activity to another. Therefore while sedimentation rate readings have been in great part correlated with signs and symptoms present at or about the time each test was done, no hard and fast line has been drawn between these taken individually and the same/

same expressed in series. Thus no relationship can be fairly drawn between one sedimentation reading and the weight of a patient at that time. But taken over a period there is a relationship between progress of the lung lesion and progress in the patient's general condition as expressed by a curve of his weight. A similar comparison has been drawn between the sedimentation rate curve and the more vexed question of presence or absence of bacilli in the sputum. Delmege (28) has divided what he terms criteria of progress into those accurately measurable and conditions of which only a general idea can be formed. His first class included pulse, temperature, sputum and weight. These can be compared with sedimentation rate values either individually or as curves. Those not accurately measurable constitute progress either one way or another taken in conjunction with the first group, and as such can be correlated with a curve made up of sedimentation rate readings plotted successively.

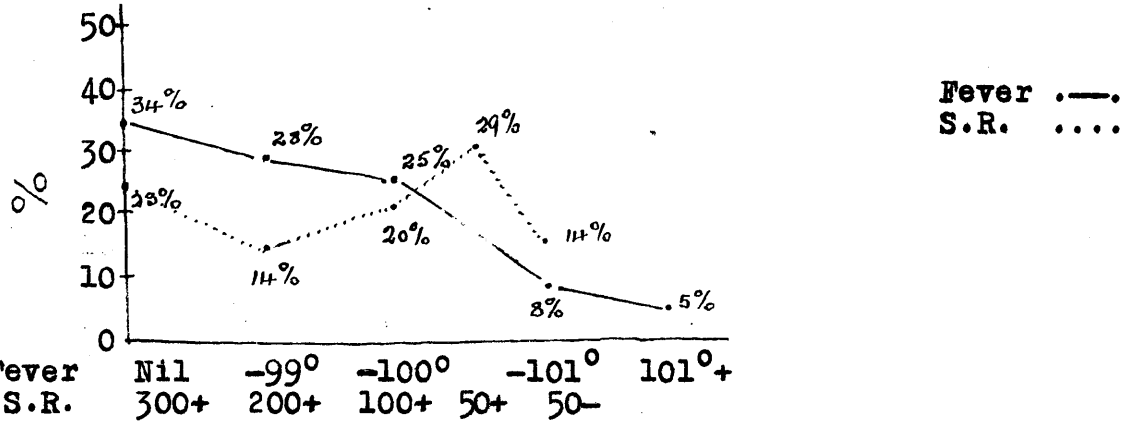
(B) IN RELATIONSHIP TO FEVER.

Table 2.

Mean peak fever	Sedimentation Rate (in minutes to fall to the 18mm. mark) 300	200-300	100-200	50-1000	-50	Total
No fever	44	16	9	10	1	80
- 99°F.	7	17	24	18	1	67
99°-100°	3	1	13	30	12	59
100°-101°	-	-	2	6	10	18
+101°F.	-	-	-	4	9	13
Total.	54	34	48	68	33	237

An attempt has been made to correlate the sedimentation rate and temperature in Table 2 above, taking each sedimentation rate reading as an individual case. Such an attempt must needs be comparatively crude, and in the table given the temperatures are obviously only approximate. Each temperature reading represents the main peak temperature whether the rise be in the evening or in the morning as happened in several cases, over a period of about seven days round about the day on which the test was done. Any complication arising likely to cause a definite rise of temperature has been taken account of, but only in a very few cases has the succeeding rise of temperature been excluded. Thus in one man a rise due to a proven non-tuberculous appendicitis which developed a few days after a certain sedimentation rate reading has been ignored. Similarly the effects of vaccination, which, though theoretically compulsory in every patient in the investigation was practised only during a period when it seemed urgently desirable, were ignored, and the temperature assessed on a period immediately preceding the resultant rise. Thus of the 237 observations, 34% had no associated temperature disturbance, 28% showed a mean peak temperature between normal and 99°F, 25% between that and 100°F, 8% showed fever of over 100° and less than 101°F and 5% fever over 101°F/

101°F. An investigation on the same lines shows that of the total of 237 sedimentation reactions 23% took over 300 minutes, 14% between that and 200 minutes, 20% between 200 and 100 minutes and 29% between 50 and 100 minutes. The remaining 14% took less than 50 minutes to reach the 18 mm. mark. These figures graphically represented are shown in chart 1.



These graphs are however not intended to be taken as sources from which final conclusions might be drawn, but represent the ratios of varying degrees of fever and of types of reaction. There is, however, a certain parallelism in the distribution of the cases, but with this important difference in the distribution of the cases, that in the temperature curve the frequency tails off towards the "ill" end, while the sedimentation rate curve is one of negative skewness. The impression thus formed might therefore be that over all the sedimentation rate paints the gloomier picture.

The whole question can however be more fully studied by separating/

separating the two curves and studying each factor as related to the other. The actual influence of temperature as such on sedimentation has given rise to diverse published opinions but Willis[29] quoting Morriss states that "elevation of the patient's temperature does not affect the rate of sedimentation".

Table 3.

Cases 237	% Sedimentation Rate Normal.	% Sedimentation Rate Pathological.
No Fever (80)	75%	25%
Subfebrile (67)	34%	66%
Fever+ (90)	4%	96%

For the purposes of Table 3 above only gross changes in sedimentation rate are dealt with. The limit set for normal cases was 200 minutes which is admittedly low, and which, were sedimentation an accepted and reputable test of activity, would include some cases not quite inactive. Such cases will, however, be gone into later.

Table 3 shows that of 80 readings unassociated with fever, 75% gave a"normal" sedimentation rate, and 25% a rate which was definitely and considerably accelerated. The low rate in the 25% may be taken either as evidence against the reaction or strongly the reverse. A similar position is shown and discussed by Frimodt-Moller and Benjamin[30] who explain/

explain it by saying, "as Westergren points out, that the sedimentation test usually keeps moderately high for some time after the fever has subsided, up to one month or more". A reference back to Table 2 shows that this 25% is however constituted of 9 readings below 200 and above 100, 10 between 50 and 100, and one as low as less than 50 minutes. These latter two groups seem particularly difficult to explain even on the basis suggested by Westergren.

The second group of 67 cases were graded as subfebrile, and is composed of cases in which the temperature was above normal yet below 99°F. Of these cases 66% gave a grossly pathological result, but the remaining 34% came under the modified normal classification. This rather large figure suggests that in what is really the very type of case in which such a reaction might help, no such help can be guaranteed, and that in one case in three the test not only fails to help the clinician, but may actually mislead him. (30) Similar cases are reported by Frimodt-Moller and Benjamin. If, however, the normal reading suggested by Linzemeir is rigidly enforced there can be deducted 9 sedimentation rate readings associated with slight temperature disturbance and which fell between 200 and 250 minutes. This reduces the 34% to 22%, a still considerable possible error.

When, however, the definitely febrile group of cases is dealt/

dealt with 96% of them are found to have low readings, the remaining 4% coming into the normal group. This 4% can in no way be reduced and must stand as a definite group of cases in which absolutely no relationship can be found between temperature and the sedimentation rate. This disagrees widely with the findings of Schmidt (31) working on 189 cases and using the same technique. In his paper he admits to several normal readings, but states that in no case were they associated with fever.

Table 4.

Cases Showing	% No Fever	% Subfebrile	% Fever
Sedimentation Rate Normal (89)	68%	27%	5%
Sedimentation Rate Pathological (148)	14%	29%	57%

Dealing secondly with sedimentation values as compared to temperature a comparative table is shown. Thus, adopting the same standard as normal or closely approaching normal, 89 cases may be so classified. Of these 68% were unassociated with any fever, 27% showed a definite though slight temperature disturbance, 5% showed gross fever. As in Table 3 a correspondence is shown in the majority, and a definite though small fraction is present which is inexplicable, if the two gauges of activity be equally assessed. Thirty-

Thirty-two per cent of the normal readings were associated with fever and as in the last group constitute the anomaly. Krimphoff (32) discussing 12 similar cases seems to lean to the sedimentation rate as being more accurate and suggests that a persistent subfebrile temperature need not indicate activity. By close investigation this group may be reduced. Reference to Table 2 shows that 34 readings or 14% of the total number done on pulmonary cases are loosely grouped as falling between 200 and 300 minutes. Of these 34 cases 19 can be more accurately placed as falling between 200 and 250 minutes or according to Linzemeir's standard, in a group which is immediately below normal. Ten of these cases were unassociated with fever and 9 were accompanied by a temperature of less than 99°F. No cases in this subgroup were associated with any higher temperature. Among those cases having strictly normal sedimentation according to Linzemeir's standard such a transference raises the percentage of cases having both normal sedimentation rate and no fever to 74% but still leaves a definite and incontravertible 21% which have slight fever, the 5% having definite fever remaining as before. The cases transferred constitute a group in which the sedimentation rate may be looked on as doubtful; though coming extremely close to the normal. Of those doubtful cases between 200 and 250 minutes taking/

taking Linzemeir's figure of 250 minutes as the lowest normal, 50% showed no associated fever, 45% showed slight fever and 5% showed fever over 99°F. The last group containing those cases with a frankly pathological sedimentation rate remains as tabulated. In it 14% of cases having a pathological sedimentation rate showed no temperature disturbance, 29% showed slight fever, and the remaining 57% showed definite rises of temperature above 99°F. In the first group of 14% commentary similar to that made on Table 3 might be put forward. Possibly such cases might be used as evidence of the greater accuracy of the sedimentation rate as an index of activity and a striking case to show this is reported by Tegtmeir.(25)

Summing up, therefore, one cannot avoid coming to the following conclusions. So far as one is aware the patient's temperature is a definite and trustworthy index of the progressiveness or quiescence of his lesion, a statement about which numerous writers could be quoted, and any test for which it is claimed that it will demonstrate finer shades of activity or bring to one's cognisance cases previously deemed quiescent, must in the first instance be rigidly tested against the known and accepted gauge. In the comparison of temperature with sedimentation rate one would be justified in supporting the claims once made for

the/

the latter, if only the present investigation did not show in both Tables 3 and 4 a considerable group of cases in which the sedimentation rate suggested frank quiescence, the temperature alone and quite apart from pulse and general consideration did not emphatically state the opposite. That there is a correspondence in the main cannot be denied and an obviously active case will in all probability give a low reading, but if a small percentage of known active cases is found to give normal sedimentation rate readings, the case for the test as superior to the temperature as an index of activity falls to the ground. Such proof alone seems sufficient, but when one deals with the large numbers of patients who suffer from such lesions as give only slight and perhaps intermittent temperature changes, further fault can be found. In such a group the blood sedimentation rate may be only slightly accelerated, and in numbers of cases almost normal, as has already been remarked. It is in cases of this sort that help is most needed and the present investigation based in this instance on individual readings and the corresponding temperature levels, seems to prove, that while in some it may help, in others the sedimentation rate is too optimistic, and in the remainder it merely agrees. It is therefore valueless. As has been previously stated two curves, one of temperature and/

and one of sedimentation rate readings, might show correspondence or even help, and such curves will be discussed later under the patient's progress generally.

(C) RELATIONSHIP TO PULSE RATE.

In the next table (Table 5) some attempt has been made to compare the sedimentation rate with the pulse rate on the same lines as were used for the temperature readings. There seems to be a considerable body of clinicians who place great reliance on the pulse rate as an index of quiescence or activity, and some who prefer a chart of the pulse to one of the temperature. There seem to be definite grounds for their belief in many cases. Patients are commonly met with who, while in bed or after a period in bed, show no temperature disturbance, but who suffer over a long period from a degree of tachcardia, persistent or intermittent, and a similar condition of affairs may persist after exercises have been commenced. It is difficult to say exactly when any one pulse is too fast, unless the patient's average normal pulse rate is known. Guy (33) states "one should consider an average pulse of over 85 in men and over 90 in women to be abnormal", and for some time past the writer has made use of this criterion. In children however reliance must be placed on the tempera-

ture/

temperature alone. The writer makes no attempt to disparage the temperature chart in view both of his own experiences, and those of his teachers, but he feels that in many cases just on the border line of activity, the pulse rate curve will prove of considerable help.

Fishberg (34) dealing with prognosis states "excepting in heart disease and hyperthyreoidism, no disease can be valuated prognostically with the same degree of accuracy by the pulse rate as chronic phthisis..... Tachycardia is an indication of the acuteness of the process or of low resistance or both". Kingston Fowler (35) remarks too, that pulse curve and temperature curve may not closely follow each other, but that "frequency of the pulse is influenced more by the strength of the patient than by the degree of fever". Very similar views were expressed by Drs. Crocket and Munro in the discussion following a paper read by Dr. A. Morrison McIntosh (36) at the November, 1929, meeting of the Tuberculosis Society of Scotland. Smith (37) used the pulse rate as a control during the treatment of twenty cases of phthisis by heliotherapy, and he is of the opinion that compared with the temperature as an index of activity the pulse compares very favourably. Delmege (28) after discussing the liability of the pulse to be upset more easily than the temperature, says "I have found it quite as helpful as the

temperature/

temperature curve, less liable to error, and of the greatest help when considered in conjunction with other evidence...." He sets the limit of normality at 80 for men and 90 for women.

Table 5. (which excludes all patients under 18 years old)

Average pulse	Sedimentation Rate (in minutes to 18mm mark).					Total
	300	200-300	100-200	50-100	-50	
+110	-	-	1	8	14	23
100-109	1	3	9	26	12	51
90-99	5	7	15	14	5	46
80-89	18	8	13	1	2	42
70-79	9	1	2	-	-	12
-70	-	-	-	-	-	-
Total	33	19	40	49	33	174

The above table comprises 174 readings of the test with their corresponding average pulse rate for the period about which each reading was done. It shows a drop of 63 readings from Table 2; these readings having been done on the 17 patients under 18 years old which are excluded.

Again at first sight it is obvious that a certain degree of correspondence exists, since high pulse rates increase as sedimentation becomes faster; and the bulk of the more normal rates are grouped with normal or just subnormal sedimentation readings. Of those with a pulse rate below 80 per minute 75% showed clear normal readings, 8% showed an associated reading/

reading which is still good though not so definitely normal and 17% showed a sedimentation rate which was pathological sedimentation. Associated with pulse rates above 100 per minute, only 1% gave normal readings, 4% readings close on normal and 95% gave definitely pathological readings; on the whole a fairly convincing correspondence. Again, however, it is to be reiterated that there is little difficulty in saying that these latter cases are active; blood sedimentation merely confirms and does not help. Among those patients with a pulse rate between 80 and 100, as in those with slight temperature disturbance, one expects help from the test, and does not get it. For among them, only 57% had fairly low readings and 17% readings on the border line. The remaining 26% had definitely normal rates of fall.

Accordingly without going at length into arguments promulgated when discussing the possible association between fever, as a sign of activity, and the blood sedimentation rate, it is seen that the position arising from pulse and sedimentation rate comparison is strictly comparable. A group exists in which it is conceivable that the sedimentation rate warns that other signs do not truly show the state of affairs but it is only in a small percentage. Another group is found in which both are sufficiently definite as to leave no shadow of doubt, though even there a small number of readings disagree/

disagree. But in the main groups, in the patients commonly met with, the position is not at all so clear cut. Omitting all reference to the 17% border line readings, the 26% with normal rates and a degree of tachycardia is insufficient to justify the supplanting of the pulse rate, a known accurate guide, by a test about which conflicting opinions are yet expressed.

Having discussed both temperature and pulse in their relationship to the blood sedimentation, one has disposed of both the accurate guides to activity and the investigation seems to show that the sedimentation rate can in no way displace the ward chart. It is conceivable that much use might be made of an isolated test, where neither temperature nor pulse records over a short or long period were available, since in the majority of cases it corresponds. One concludes therefore, that since discrepancies are present it cannot be relied on as a test of activity, a statement emphatically disagreeing with the findings of Clegg (38), and certainly it cannot compare with temperature or pulse records. These conclusions are the antithesis of those published by Motzeldt (39). Taken in conjunction with ward records, some help may be derived, but in the event of disagreement and in the absence of some extraneous cause for disturbance, reliance were better placed on the common signals of activity.

(A)/

(A) RELATIONSHIP TO WEIGHT.

Other signs and symptoms of activity do not lend themselves so readily to tabular comparison. Increase of weight may or may not denote cessation of activity or even may not represent progress, The presence of tubercle bacilli in the sputum is too debatable a sign of activity to compare mathematically with sedimentation rate readings. But, on the average, gain in weight followed through regular weighings is a good sign, as is the diminution or absence of bacilli from the sputum; both represent a degree of progress and as progress they will now be studied in relationship to the sedimentation rate.

Table 6.

Weight	Sedimentation Rate			Total
	Improving.	Becoming Faster.	Steady or Slightly Variable	
Rising	16 or 69.5%	3 or 13.1%	4 or 17.4%	23
Falling	———	16 or 76 %	5 or 24 %	21
Steady or Slightly Variable.	7 or 41.2%	7 or 41.2%	3 or 17.6%	17

Table 6 above shows roughly the relationship between alterations in weight and in sedimentation rate. Of cases with improving weight about 31% show no improvement in sedimentation rate, and this figure includes 3 cases in whom the reaction

suggested/

suggested loss of ground in spite of gain in weight. In the second line of the table the noteworthy feature is that no case was found who had falling weight and an improved reaction. The majority of cases losing ground show rapid sedimentation, and the remainder remaining variable. The remaining 17 cases whose weight altered little or nothing are fairly equally divided between cases with improved and poorer rates. The table is made up of serial readings and weighings of 61 cases on whom the test was done at least twice. The outstanding fact is that no patient losing weight showed slowing up of the sedimentation rate. Primodt-Moller and Benjamin (30) point out a precisely similar state of affairs and also show figures comparable to the first line of Table 6. Further investigation of Table 6 gives little more information. It might be mentioned, however, that of those cases in whom the weight increased, none ever reached a weight proportionate to their height and general conformation, in whom the sedimentation rate fell or remained steady; whereas a large number of those whose physique improved synchronously with their sedimentation rate, reached and maintained, so far as can be known, a weight which for them was normal. Similar comment can be offered on the other sub-sections. Further, those whose sedimentation rate was fast at the outset and slowed up only gradually - for example taking 100 minutes or less - were found/

found to supply the largest number of cases in whom weight increase was slow, and who finished much below weight; and conversely those whose sedimentation rate at the first time of testing was increased, but not markedly so, were found to make good any weight loss and to maintain it fairly consistently. Those patients whose blood cells fell in 50 minutes or less rarely gained in weight to any great extent though usually the sedimentation rate improved considerably, albeit in no case reaching normal. One case was found, however, who during a residence of 12 weeks (approx) gained 19 lbs. and whose initial reading was 30 minutes and 2½ months later 146 minutes. Further reference will be made to those facts when progress as a separate entity is dealt with.

(E) IN RELATIONSHIP TO SPUTUM EXAMINATION.

Generally speaking the mere presence or absence of tubercle bacilli in the sputum gives no definite information as to the state of a known and accepted tuberculous lesion. Many patients are met with who throughout their residence in a sanatorium fail to give a positive sputum and a certain number of these can definitely be labelled active by other criteria. Similarly chronic lesions in patients able to work may demonstrate persistence of a T.B.+ sputum without any obvious recrudescence. But while the presence or absence of bacilli cannot solely be used/

used to assess activity the gradual diminution and final cessation, or the gradual increase of bacilli in the sputum has a definite significance. Fishberg[40] says "there are cases which show but few bacilli in each specimen yet they run an acute and progressive course, while others with numerous bacilli pursue a slow chronic course terminating in recovery..... On the other hand, the complete absence of bacilli from the sputum for several weeks coupled with improvement in the general condition of the patient is undoubtedly a favourable sign." Dealing with another aspect of the question, the same writer, quoting Bardswell, says "there is no doubt that the chances of improvement and survival are larger in sputum negative cases....." In a similar strain Fowler writes "If tubercle bacilli appear while the patient is under observation that fact alone..... reduces his expectation of life for the time during which they are present". Guy[41] quoting the standard of the American National Association says however "absence of bacilli in the sputum after one or several laboratory examinations is not necessarily proof against the presence of active tuberculosis". Paterson[42] writes in like vein on his own and other experiences and concludes by saying "The value of a positive tubercle bacilli examination is that it proves/

proves infection and that is all that should be accepted from this evidence". In contradistinction to the last remark, finally Burrell's (43) statement might be quoted in which he says "tubercle bacilli in the sputum are definite evidence of infection and may be taken as indicating active disease".

Table 7.

Sputum at 1st Test.	Average Reading (in minutes).	% Normal Readings.	% Subnormal Readings.
T.B.+	113 minutes	14%	86%
T.B.-	251 minutes	50%	50%

It so fell out in the investigation that of the 72 pulmonary cases, 50% had no bacilli in their sputum or had no sputum, and 50% had bacilli present when the first reading was made. In the small generalised table above no account is taken of the number of bacilli present. It is found that T.B.+ patients have very definitely a low reading (113 minutes), but it is to be remarked that 14% of such cases had normal readings. This disagrees with Westergren who has not found a case with T.B.+ sputum and a normal blood sedimentation but it shows a close resemblance to figures published by Frimodt-Moller and Benjamin. (30) As opposed/

opposed to the low reading (11¾ minutes) of T.B.+ cases, there is the normal average reading of T.B.negative cases (251 minutes). Of these 50% showed normal readings and 50% abnormal. This again closely corresponds to Frimodt-Moller and Benjamin's figures though differing rather widely from the figures published by Trail and Stone (16) who show a much smaller percentage of normal readings among their T.B. negative cases. The matter looked at in a wider clinical vein shows that 83% of the T.B.+ cases were certainly active when the first reading was done and the remaining 17% if not inactive almost so. Similarly with the T.B.- cases; roughly half were active and half were more or less quiescent. It would certainly seem therefore that rapid sedimentation rates are more often than not associated with a positive sputum, but if the sputum be negative, the sedimentation rate may be high or low, and again give little help.

Table 8/

Table 8.

Sedimentation Rate Levels at 1st.test & Rise or Fall in minutes.	Sputum on first and last readings				Totals.
	1 2 + +	1 2 + −	1 2 − +	1 2 − −	
150–300 and rising	1	2	−	6	9
− −150 and rising	9	5	−	4	18
Steady above 150	−	1	−	7	8
Steady below 150	4	−	−	−	4
300–150 and falling	2	2	2	2	8
150− − and falling	6	2	2	5	15
Totals	22	12	4	24	62

Table 8 above shows what relationship there is between the sputum examination at the beginning and end of the investigation of each individual, and a rise or fall in the rate of sedimentation. In column 1 it is to be remembered that rise or fall refers to minutes or to time taken; thus "150–300 and rising" means that the first reading lay between 150 and 300 and thereafter the time taken rose, or that sedimentation rate fell, or in short the change was a good one. The table was compiled from the readings of the

62/

62 cases who were tested at least twice. While the numbers are small, the outstanding feature of the table appears to be that no cases were found in which the bacilli were absent at the beginning and who, at the termination of the research, offered a positive sputum, in whom the sedimentation rate changes for the better. Again it is to be noted that most of those admitted positive and still positive at the time of the last reading are to be found among low readings; there being little difference whether the sedimentation rate became slower or faster. Of those whose first examination showed bacilli and whose last failed to, little difference can be made out on any point, the whole number being fairly evenly divided between readings higher than average and those lower, and between slowing and accelerated rates. Similarly a summary of those admitted negative and still negative at the last examination is inconclusive. Notice might be drawn to the fact that of 24 such cases 13 were associated with readings of 150 minutes or over which either rose or remained roughly stationary. Against that there is the occurrence of 5 cases below 150 minutes who come into the same category. Finally, and quite apart from Table 8, it was found in a few cases whose sputa were labelled ++ or +++, following the method advocated by Crockett, that for those with sputa marked +++ the highest

reading/

reading was 37 minutes and for those marked ++ 103 minutes.

Summing up, it is difficult to stress the claims of either sputum examination or the blood sedimentation rate as a gauge of activity since there is no unanimity on either. In the average case with a positive sputum the rate may be normal in a few, but low in the majority; and apart from the notice drawn to the third column of Table 8, the progress of the case so far as sputum examination is concerned, does not necessarily bear any relationship to the upward or downward trend of the blood sedimentation rate. Dealing solely with cases having a negative sputum the issue is still more confused. While the average for such cases was normal in the investigation, it appears to have been the average for a group of inactive cases, a group of very active cases, and a group about which it might be said that they were perhaps transitional but yet definitely active. These latter very active though T.B.- negative cases show readings only slightly higher than the cases cited above as T.B.++ or T.B.+++ and so little significance can be attached to the incidence of the latter, striking though it be. It would therefore seem that there is no marked relationship between the presence of bacilli in the sputum and the blood sedimentation rate. The latter is under examination and it seems/

seems unwise to dissociate the former from any case taken as a clinical whole, since even a very active case, with an agreeing sedimentation rate may yet lack bacilli in the sputum.

THE TEST IN DIAGNOSIS.

Most of the evidence of workers in the past of this investigation has tended to show that the blood sedimentation rate affords little help in deciding whether or not any individual lesion is or is not an active one. Even Westergren's statement that in the presence of a normal reading a phthisical lesion could not be active in the ordinary sense of the word, seems now to be disproved. Other diseases have been mentioned in this paper in which it is now realised that an accelerated rate is found. It follows therefore that the importance of the test as a diagnostic must be limited.

The administrative arrangements whereby the material used in this research were admitted to the wards concerned, were such that few patients were admitted but who suffered from tuberculosis. Accordingly any findings are based on very limited material. They are appended as individual cases with readings, and criticism offered.

1/

1. W.McP. aged 50: admitted suffering from tuberculosis of the humerus with sinus formation. Temperature range during first week of residence 98°F to 101.4°F. Pulse rate average 100-110. Severe cough with purulent sputum, said to be the result of long standing bronchitis. The chest showed some emphysema, and areas of fibrosis at each base with numerous coarse rales. Radiogram reported "peribronchial fibrosis with basal bronchiectasis and some interlobar pleural thickening". Sputum persistently negative, urine free of all abnormal constituents. Blood sedimentation on admission 14 minutes to the 18 mm. mark. This man's arm made no progress either way, and his chest remained as on admission. Within six weeks of admission he developed intermittent and later persistent sickness. Later still epigastric pain. Gastric contents showed complete absence of hydrochloric acid. A pyloric carcinoma was diagnosed and found to be inoperable. He lived about two months longer and the diagnosis was confirmed post mortem, by which time he had a diffuse carcinomatous peritonitis.

The blood sedimentation reading was one of the lowest recorded. Temperature and pulse with such a reading suggested active if not acute phthisis but the stethoscope and radiogram refuted this. Low readings are recognised in carcinoma, and on the continent in some clinics the test

is/

is routine when carcinoma in any form is suspected. Beaumont and Dodds[9] recognise the occurrence of rapid sedimentation rate in carcinoma and Alterthum[44] reports just such a case as is mentioned.

2. C.M. aged 9: this boy's history is a long one of repeated periods of cough following pneumonia when very young. Sputum was rarely obtained but when got was always negative. Temperature range on admission was up to 99°F. and at the termination of about six months' residence ranged from 97.4°F. to 98.4°F. Pulse at first 85-100 and at termination of residence 80-96 per minute. Successive readings in minutes were 360, 280, 308, 410. The physical signs were indefinite and a radiogram showed basal small tube bronchiectasis with fibrosis and interlobar pleural thickening. The report finished "Can this be post pneumonic?".

The diagnosis seems to have been post pneumonic bronchiectasis. The boy remained in hospital a considerable time, most of it spent in bed, and left comparatively well though not looking robust.

3. R.Y. aged 13: admitted from another institution with a typical right-sided pleural effusion. This evidently had been slow to be absorbed and during a long residence here was equally slow. The boy was in no way upset by its presence/

presence. He was retained about three months after complete absorption. His readings in succession were 239, 268, 253, 261, 274 minutes.

X-ray examination after absorption reported "No intrapulmonary disease" which apart from diminished right basal R.M. agreed with the clinical findings. The boy was dismissed extremely well. Was this an idiopathic pleurisy? As will be pointed out later the onset of an acute pleurisy during the course of a phthisical lesion is attended by a definite lowering of the sedimentation rate. The same statement applies to accumulation of fluid during progress of artificial pneumothorax.

No conclusions can fairly be drawn from three cases, two of which so happened to have associated high readings. Quite apart from the original purpose of the investigation, it was noticed that during a certain influenza epidemic only three patients among the cases in this ward contracted the ailment. These three were probably the most quiescent of all, and all had associated high readings done at or about the time of their complication.

THE TEST DURING TREATMENT/

THE TEST DURING TREATMENT.

1. GENERAL.

Table 9. (Compiled from the figures of 62 patients who had at least 2 readings).

Terminal Condition.	Sedimentation rate.		
	Improved.	Stationary.	Worse.
Arrested (6)	6	-	-
Much Improved (9)	8	1	-
Improved (18)	10	5	3
Stationary or worse (29)	3	6	20
Total (62)	27	12	23

The table above shows the relationship between the condition of the patients at the termination of the investigation and the change in their blood sedimentation rates. Of the 27 cases showing an improved rate, 6 or 22% were arrested, 8 or 30% much improved, 10 or 37% improved and 3 or 11% stationary or worse; in short 89% showed recognisable clinical progress and 11% either showed no change or became worse. Twelve cases showed a steady rate throughout; half of these either became worse or failed to improve. One seemed to improve greatly but he was a case having a high initial figure (in minutes). Only 3 cases out of 23 whose rate became progressively more rapid showed improvement and that of slight degree. The figures above, but for one remark, fail to take any account of the initial figure, but elastic/

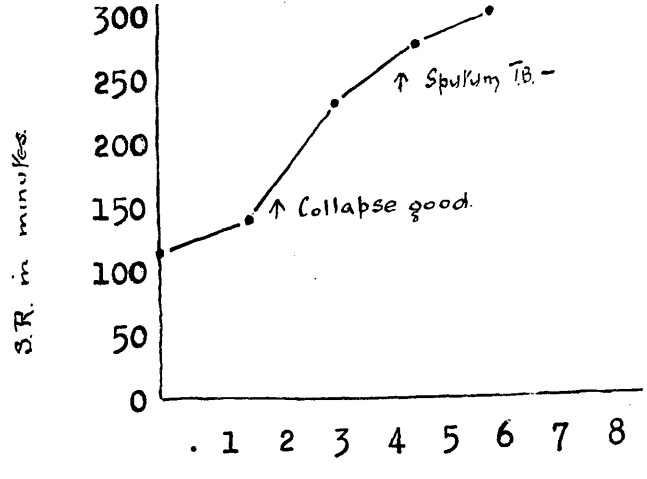
elastic as the table's scope is there seems a definite correspondence between the reaction done over a period and plotted as a curve and the change in the patient's condition as manifested clinically. It will be shown when prognosis is discussed that considerable importance attaches to the initial and early speeds, and to the type of curve resulting from successive readings but in the main it would at present seem that a rising curve is commonly found if the patient improves. It is noteworthy that of 15 cases arrested or much improved, only one did not show a beneficial change in his blood sedimentation rate, and this case has previously been mentioned.

2. IN ARTIFICIAL PNEUMOTHORAX.

The nature of the material on which the test was done was such that in only a very small number was treatment by artificial pneumothorax possible. In all collapse was successfully brought about in four cases, but one of these is excluded, since in this instance collapse was done for severe persistent haemoptysis and did not alter the course of the disease in the slightest degree. Of the other four cases two are not included in the table previously given. They were cases outwith the writer's jurisdiction but on whom he performed the test prior to induction and once again some considerable time later.

Case/

Case 1. Wm.M. aged 23 years. Admitted with active disease of the upper two lobes of the right lung. This disease seems originally to have been the result of hilus disease and outward spread, since there was some fanshaped fibrosis extending out from both roots and affecting also the right base and an area about the left root. The areas causing concern were limited to the upper two thirds of the right lung. In view of the site of the lesion in the left lung treatment was on general lines for about 6 months, but while his initial temperature and pulse range was reduced in that time, he retained a marked daily range, with slight feverish attacks and occasional peaks to 100°F. His sputum throughout remained positive. Artificial pneumothorax was decided on and induced after two attempts. As would be expected collapse was not complete, being limited by one marked band. This eventually stretched and gave way without mishap. This man has been followed as an outpatient still receiving refills.



A.P. X-ray shows good collapse

It was not until very good collapse was obtained that this man's sputum became negative; his temperature became normal, and tachycardia ceased. The one disquieting feature is that gain in weight has been disappointing and he is still as an outpatient rather under weight. His sedimentation rate done as an outpatient remains satisfactory. Cases 2 and 3. These, as has been said, are not mentioned elsewhere in the investigation, and were the only female cases on which the test was done. Both suffered from active but moderately early phthisis, (a) one of the right upper lobe, and (b) one slightly more extensive though still limited to one side. Case (a) was undoubtedly deteriorating rapidly when artificial pneumothorax was induced. Her sedimentation rate, done by request of a colleague, was 27 minutes. Collapse was successful. Recently this girl has commenced to attend as an outpatient for refills and her sedimentation rate is now about 200 minutes over two or three readings. She has no sputum and is fit and well. (b) showed even a lower first reading, and after induction the rate fell greatly. Her reading recently (and about 15 months after the first) is reported to be about 300 minutes. She too is fit and well but has some plural effusion. No reading is available to correlate with this complication.

It would accordingly seem that the reaction on the limited experience/

experience of this research does allow the clinician some concrete evidence of improvement. This is in accord with numerous writers' opinions, and some of these go so far as to say that in this branch of treatment the test is likely to prove of greatest value. This statement will be referred to later.

3. IN EXERCISE.

No scheme of graduated labour is used in the ward under observation and usually on first getting up patients are allowed to walk about the ward. Later longer walks in the grounds are permitted, and eventually they are expected to assist in ward work and do errands connected with the ward. In a very few of all the cases considered an attempt was made to correlate the temperature and pulse in exercise with the sedimentation rate. Generally speaking both seemed to be of equal value in this respect. Thus a patient who had a reading of 300 minutes was made walk two miles and temperature and pulse observations taken every 30 minutes thereafter. The temperature rise was slight and rapidly absent, but the elavation of the pulse remained for about 30 minutes longer. In another whose sedimentation rate at commencement of treatment was 112 minutes, and at the same time of the exercise test had risen to 158 minutes, the temperature rose 1.5 F. and remained above normal for 1 to 2 hours, his pulse level remaining high for a considerably longer period.

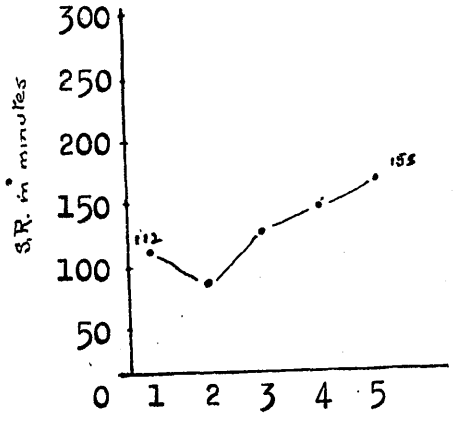
Both/

Both these instances could be repeated, but these furnish examples which suggest that an estimation of the sedimentation rate is of a similar value to exercise tests; though it seems that too many extraneous factors enter into the more commonly used temperature reaction.

4. RELATIVE TO RATE OF PROGRESS.

As has been said already in the majority of cases, clinical improvement is associated with an improved sedimentation figure, and the following instances roughly suggest that a slowly improving sedimentation rate or one which remains steady, and a rapidly improving case shows a substantial fall in the speed of the reaction.

Fig.1.



Readings.

The graph above is that of one of those cited in the last subsection and shows a poor starting figure and a slow and slight rise after between 6 and 7 months treatment. He was unable to remain longer. He was admitted with a daily temperature but with/

with a daily temperature range of 1.8°F and dismissed with a normal evening temperature but with a subnormal figure in the morning. Sputum examination showed bacilli throughout though only isolated organisms could be found at the finish; the actual amount of sputum diminished slowly. Weight gained was slight and tended to be ill maintained. This man while having advanced disease would probably have attained a much higher standard of fitness had he been able to remain a longer period.

Fig. 2.

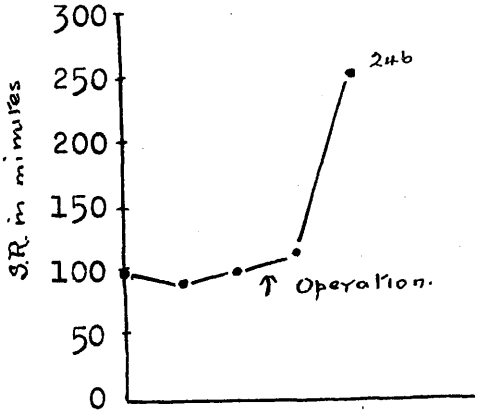
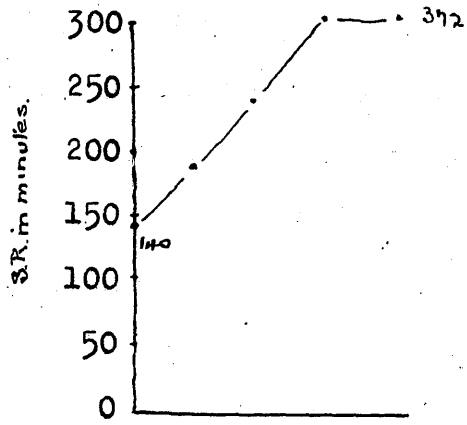


Figure 2 above is the graph of a man admitted T.B.+ with advanced phthisis tending to fibrosis, but quite definite active. In addition he suffered from tuberculosis of a knee with sinus formation, and had scars of healed cervical glands. Amputation of the leg was done between point 3 and point 4 and thereafter he made rapid progress. On admission his temperature ranged from 97°F to 100°F. and on dismissal was normal. Similarly with his pulse.

Fig. 3.



The curve above is that of a man who came under the C 2 classification. He had at first a positive sputum which very quickly became negative, though occasional positive results were obtained thereafter. Temperature disturbance was definite but not marked at point 1 and was absent within 6 weeks of commencement of treatment. His pulse was only slightly rapid at the start and finished at a normal figure.

Accordingly, without multiplying the diagrams it seems clear that the curve constituted by successive sedimentation readings does reflect the progress of a case. This holds equally well in the converse for cases which are deteriorating from any case whatsoever. This follows closely the finding of Wylie (45) done on a large mixed group of cases of tuberculosis. Generally speaking the lower the figure at the commencement the slower will be the progress and vice versa. Trail and Stone (46) have applied these curves to an estimation of the probable/

probable period during which treatment will be required, and it seems reasonable to expect that if progress be maintained at the rate a graph indicates, some idea of the future time required can be got by prolonging such a graph till normal figures be reached.

5. THE TEST IN COMPLICATIONS.

In this section only those complications the direct result of tubercle of the lung are dealt with. No account is taken of the previously mentioned non-pulmonary tuberculous complications.

Haemotysis.- Of the 72 patients tested in this research, 9 had at least one haemoptysis. All, with one exception, were G.3. cases and over all the readings were low. One man with marked cavitation and a normal sedimentation rate in spite of obvious toxaemia, died from a very large haemoptysis prior to a second reading being done. In a second, death took place for a similar reason, but for some time prior to his death the rate had been steadily becoming accelerated. With one exception, the others are uninteresting in that no change could be made out in the sedimentation rate which could be definitely put down as due to haemorrhage. The exception is interesting in that it shows the confirmatory value of an estimation following haemoptysis, particularly if large.

The patient in question suffered from advanced phthisis and tuberculosis of the spine, and had been treated for

several/

several years. For 3-4 months before the event of his sedimentation rate had been quite normal and pulse and temperature had been well settled. Sputum was minimal and negative for tubercle bacilli. Shortly before he was about to get up and while yet wholly recumbent, he took a moderately severe haemoptysis. Within a few days he showed evidence of active spread in the lung from which the haemorrhage is thought to have arisen, and a sedimentation rate estimation done about that time showed a distinct fall. He went home about two months later in a critical condition with swinging temperature and positive sputum.

Fig. 4.

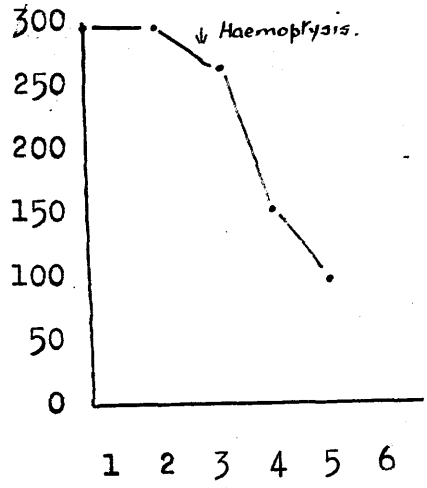


Figure 4 gives some idea of the change. It is doubtful if any significance can be attached to the slight drop from point 2 to point 3; clinically there was nothing to account for it. The marked drop between 3 and 4 and prolonged to 5 coincides with the period when he suffered from what amounted/

amounted to a tuberculous bronchopneumonia.

Possibly therefore after any haemoptysis larger than mere staining, the sedimentation rate might give early information as to any serious effects of the bleeding. In the other cases mentioned, the readings were so consistently low that had any activity arisen as a result of haemorrhage it would possibly have been missed, but occurring in a case normal up to that point, a drop in the curve such as is shown seems to make clear the exact nature of the lung process. Possibly in this man's case his enforced recumbency was largely responsible for the sequence of events.

Pleurisy.. The common finding was that ipso facto pleurisy had no effect on the rate of the reaction. In only one case which developed a large effusion, could this be associated with a depression in the curve. It is interesting that this man, who suffered from a tuberculous ankle, inactive, but with a slight sinus, improved greatly after his effusion was absorbed and the sinus of the ankle healed and remained so.

This effusion shows an entirely different reaction from "R.Y." the case given under diagnosis, where in spite of a large effusion the sedimentation rate remained normal.

In the outdoor treatment of pneumothoraces, it was found that onset of effusion was accompanied by a drop in the time taken. The matter is of greater interest than value on account/

account of routine X-ray-screening of cases at the time of refill.

Fistula-in-ano, Laryngitis etc. No definite findings can be offered here. These complications of themselves had no apparent influence on the reaction, which varied with the systemic disturbance in each case.

THE SEDIMENTATION RATE IN PROGNOSIS.

Most writers on the sedimentation rate in tuberculosis have been definite that the test offers some idea of the probable prognosis. This investigation is unfortunately based on cases, which were most of them advanced and ill, and the influence of a few cases rather out of the average is bound to be reflected in any findings offered. If it is accepted, as it was put forward by Frimodt-Moller and Benjamin (30), that the only classes of cases, with a really good prognosis, are classes A 1 and B 1, that A 2, B 2, A 3, B 3, have doubtful prognosis and that all others have poor prognosis, some previous parts of this paper may be referred to. In the group of cases used it was found that classes A and B showed good average figures, both about normal, and that class C showed a poor figure. Little difference could be found between the 1, 2, and 3, subgroups of these two classes, though observations were made at the time as to the fallacy of reaching conclusions on so few cases. In the C 1, 2,/

2, and 3 groups the averaging reading was much lower than that for A or B, and showed a steady improvement from C 3 to C 2. There were no C 1 cases. Various writers have shown a steady gradient in sedimentation rate readings from groups labelled "prognosis good", "prognosis doubtful" and "prognosis bad". In this research valid findings could fairly be drawn only from the "prognosis bad & doubtful groups", and the latter contains several cases with high readings who were classified A 3. The writer feels that the actual figures depend more on the state of the lesion rather than on its extent, and that while an initial reading may carry considerable weight, both progress and immediate prognosis are related more to the alteration in the figure for any individual patient.

Table 10.

Initial figure (in minutes)	No.	Deaths.	Losing ground.	Condition as at last reading.	Fit and working.
50 or below	7	4	—	2	1
51-100	22	12	6	2	2
101-200	14	2	4	5	3
201-250	5	—	2	—	3
250 & above	17	3	—	4	10
Total	65	21	12	13	19

The figures above are relative to 65 of the 72 cases which have/

have been traced since the last test was done on each of them. Seven of the total cannot be followed up for various reasons. Many of the total are still in the ward about one year after the termination of this group of tests, and the headings represent the condition of them and of the others at the same time. It will be seen that within one year 4 cases out of 7 with readings of 50 minutes or below are already dead and 12 out of 22 with readings of between 51 and 100 minutes. Of those registering between 101 and 200 minutes 2 are dead, and out of 22 readings above 200 minutes there have been 3 deaths. Of the last three deaths one died of a non-tuberculous complication, one was the case cited under haemoptysis and the other (also mentioned) died directly from haemoptysis. Similarly looking at those fit, or working or at school only one case below 50 minutes is recorded out of seven and in his instance clinical and sedimentation improvement were rapid. By far the majority are among those whose initial reading was satisfactory. The other columns need no comment.

It would thus seem that so far as concerns immediate prognosis a low initial reading is of bad import and a higher figure suggests at least temporary restoration to fair health. The fact that 16 deaths out of 21 occurred among the very low readings is particularly significant.

Westergren/

Westergren working over a period of 2 to 4 years after dismissal has come to a similar conclusion. Just how far ultimate prognosis might be foretold cannot be given since only 12 months period is covered by table 10.

SUMMARY AND APPLICATION. (PULMONARY TUBERCULOSIS)

The conclusion reached on the tests done on the pulmonary group may be summed up as follows

(1) It is not an accurate test of activity. In definitely active cases an estimation of the sedimentation rate will confirm in the majority, and in the quiescent cases will probably agree. In other cases between these it is quite inaccurate. This over all agrees closely with Dunlop's (47) findings on cases closely resembling those used in this group.

(2) It cannot displace either temperature or pulse curves as a test of quiescence.

(3) There is probably some relationship between the reaction and the increase, dimunition or cessation of bacilli from the sputum, but it is of little clinical value.

(4) It bears a close resemblance to weight curves, if they too are expressed serially.

(5) Following from (3) and (4) it seems therefore to give a fairly accurate idea of a patient's progress, and of response to treatment.

(6) No personal conclusion can be reached on diagnosis. An extremely/

extremely low reading in the absence of obvious causes should raise the question of malignant disease, whether it be yet clinically evident or not.

(7) It seems to have a definite bearing on prognosis. This applies to initial readings, and to alterations in successive readings.

(8) Probably, therefore, apart from prognosis, the test might prove of value as a rough and ready substitute for the ward chart but only when such is not available. As such it might be useful in dispensary practice of any sort. The writer has got some help from it as applied to patients coming for refills of artificial pneumothorax.

(B) NON-PULMONARY TUBERCULOSIS.

In all the test was performed on 71 patients suffering from non-pulmonary disease, either alone or as the chief lesion. As will be seen from the table following, by far the majority of these suffered from tubercle of bones and joints. The table excludes 6 cases of frank amyloid degeneration. These too were bone and joint cases.

Table 1./

Table 1.

Age	Site of principal lesion. Spine and Sacroiliac	Hip	Knee & elbow	Other bones & Joints	Abdomen	Genito-urinary	Glands & skin.	Total
-10	6	6	2	1	3	1	1	20
-20	8	5	4	4	2	2	1	26
-30	7	1	3	-	-	1	2	14
30+	2	-	2	-	-	-	1	5
Total	23	12	11	5	5	4	5	65

At the same time the table shows the age grouping. It will be noticed that 46 of the total of 65 cases were less than 20 years old. The total number of tests done on these cases was 215 and they were distributed as follows:-

Table 2.

Site of lesion.	Patients	Readings	Average	Highest	Lowest.
Spine & Sacroiliac Jt.	23	89	295 mns	607 mns	28 mns
Hip.	12	48	318	584	47
Knee and elbow.	11	33	246	580	52
Other joints & bones	5	18	259	349	92
Abdomen	5	8	124	279	40
Skin & Glands	5	7	321	503	216
Genitourinary	4	12	403	574	110
Total.	65	215	279	607	28

K26
E7

The outstanding features of the work done on the non-pulmonary cases were the occurrence of a general average very much higher than that for pulmonary patients and the occurrence of considerably higher figures all round. Among the low figures however there were many quite as low as the lowest readings for phthisis. Probably no legitimate conclusions can be drawn from the classification and averages given above, but two points might be made. The first is that the averages for each lesion fall quite close to one another, with one exception. The exception constitutes the second point and is the low figure recorded for abdominal tuberculosis. It is also noteworthy that both the highest and lowest readings recorded (exclusive of cases of amyloid disease) are to be found amongst those for tuberculosis of the spine. The whole synopsis above is suggestive, though not conclusive, of the lack of any definite relationship between the actual extent of the disease and the sedimentation rate; and if it so happened that the lowest readings for each type of lesion had been got from proven active lesions, some case might be made for the suggestion that the readings are low in proportion to the intensity of the focus. This will be gone into later.

BONE AND JOINT TUBERCULOSIS/

BONE AND JOINT TUBERCULOSIS.

(a) IN AMYLOID DISEASE.

One point arising from the work on those patients is gone into immediately as the results seemed to be quite definite and distinct from all others. That point is based on the 25 readings done on 6 cases of amyloid degeneration, and are of sufficient importance to be dealt with separately. As already mentioned, these six cases do not therefore come under the table previously given. The outstanding feature of those cases was the very rapid fall of the blood cells and the persistence of this rapid rate over several readings done at the usual intervals of 6 weeks. All 6 were cases of bone or joint tuberculosis of long standing and all of them showed marked chronic sinus formation. Over these 25 readings the average reading was 23.5 minutes to reach the 18 millimetre mark. The highest reading recorded was 77 minutes and the lowest 17 minutes. In every test it was noticed that fall was so rapid that the line of demarcation between the corpuscles and the clear fluid above was indistinct and readings were taken from the level from which the corpuscles were definitely massed. In addition many of the tubes showed distinct haemolysis, the supernatant fluid being definitely stained by free haemoglobin. Neither of these features had not occurred

in/

in other cases, but in amyloid disease they were so constant as to merit separate mention and either one, and chiefly the gradual merging of clear fluid and solid corpuscles, together with a very rapid rate, seem to be associated with amyloid degeneration.

The findings recorded above were got from definite cases; all of them having definite albuminuria persistent over a considerable period, some palpable enlargement of the liver and often also of the spleen, and most of them ran hectic temperatures. Other cases not showing these sighs, but yet showing low figures, seem to offer a definite application of the test. Recognising the hopelessness of such a condition as the 6 definite cases showed, some benefit might be derived from the test were it found that in the absence of some other definite cause, low readings were being recorded, prior to the onset of such features as albuminuria, liver enlargement etc. In several cases such as have been suggested, but of later date than this research, the writer has urged operative interference with a view to providing better drainage on the grounds of extremely rapid sedimentation alone. Unfortunately the cases so dealt with have all been advanced and had sinuses present for considerable periods prior to admission and so far the results have not been encouraging and in most have failed to stall off the onset of chronic albuminuria. Nevertheless a

persistently/

persistently low sedimentation rate in a case of long standing surgical tuberculosis seems as definite proof of the onset of degenerate changes in the viscera as do the most common sighs of such change, and seems to offer the surgeon an earlier or further proof that the condition is rapidly becoming incurable.

(b) RELATIONSHIP TO ACTIVITY.

In bone and joint tuberculosis the means of assessing activity are very different from those employed in the treatment of pulmonary cases. As was said before, the ward chart offers definite information as to the degree of toxaemia, but usually in an uncomplicated case temperature and pulse are firmly settled many months or even up to a year and a half before total quiescence of the local lesion. In forms of the disease not affecting bones and joints or lungs, such as renal phthisis, tuberculous peritonitis, lupus and adenitis, the usual methods may be followed; but in pure surgical tuberculosis other means have to be adopted. By some writers the body weight is looked on as a safe index of the degree of progress, but even among those cases here dealt with regular weighing was not made use of except among the ambulant patients; and even there it seemed that increased body weight was more a measure of the patients general reaction to treatment than of the activity/

activity of the lesion. Brusquely put it seemed unreasonable to carry partial immobilisation to the extent of getting patients moved and weighed. Accordingly while due attention was paid to the ward chart and the general nutrition of the patient, the methods used in those cases were mainly physical and radiological; physical methods showing the recovery of passive painless movement and diminution of spasm, and radiological methods confirming, and, in most cases amplifying the physical findings. Accordingly the patients were deemed inactive when the radiograms concurred; to modify Rollier's statement "We let the patients up when the X-rays say so". As previously stated the test was applied to these patients to see if possible even the infrequent examinations and movements involved in radiography could be further reduced.

It is obvious therefore that no tabular comparison can be offered other than a comparison of the sedimentation rate readings and the activity or quiescence of the lesions. It seems more fitting that alterations in individual readings over successive tests is more likely to be akin to healing or progress and as such will be separately dealt with.

Table 3./

Table 3. Major lesions - Spine, hip, knee & sacroiliac joints.

State of Lesion.	Sedimentation Rate (in minutes)				
	300+	200-299	199-200	-100	Total
Quiescent	42	20	1	3	66
Not Quiescent	22	8	33	34	97
Total	64	28	34	37	163

In table 3 above, as in the pulmonary tables, each reading is correlated with recorded state of the lesion at or about the time of the test. Thus if each entry or reading be looked on as a separate entity, it is seen that of 66 quiescent lesions 62 or 94% give normal readings or figures very closely approaching normal. The three discordant readings were gone into very closely. Two must remain unexplained; the third was a quiescent spine returned from an isolation hospital after having had scarlet fever. The position of those cases deemed not yet quiescent is not so satisfactory. Of the 97, close on 70% showed readings more or less in keeping with clinical condition at the time. The remainder disagree, and no great amelioration is got by the slight lowering/

lowering of the normal figure given in the table above; 22 cases showed not only normal readings but included several which were higher than normal. Possibly the term "not yet quiescent" is too severe and many of these entries might perhaps concern cases which in reality were approaching total inactivity but as the whole future of a patient with surgical tuberculosis depends on the proper realisation that the local lesion is not yet sufficiently quiet to permit of ambulant treatment, it would seem safer to depend on clinical methods rather than on a single estimation of the blood sedimentation rate. Over a number of serial readings information can be gained as will be shown shortly; but the value of a single reading in major cases is much as in phthisis. Nevertheless from the figures above it seems advisable that a case clinically inactive, yet having a low sedimentation rate should be carefully reviewed again, since such a small percentage of cases which are truly quiescent show abnormal figures.

Table 4/

Table 4. Minor lesions - Elbow, wrist, tarsus, dactylitis etc.

State of lesion	Sedimentation rate (in minutes)				Total
	300	200-299	199-200	-100	
Quiescent	4	2	-	-	6
Not Quiescent	6	7	5	1	19
Total	10	9	5	1	25

The small table above is practically self explanatory. Concerning as it does patients who on the average show practically no constitutional symptoms, one would expect the readings to be fairly high. In those quiescent this is strictly correct. Among the patients active at the time of reading only slightly over 30% showed a real lowering of the falling time; the remainder while clinically definitely active still gave normal readings. It is obvious therefore that for smaller lesions the test is useless. Little importance need be attached to such a finding since such cases are more easily assessed than the previous group and the results of reaching a faulty opinion on the lesion are not so serious.

Little therefore remains to be added to the commentary on table 3. The investigation shows that clinical methods, since they are certainly the safer, should clinical methods, since they are certainly the safer, should not/

not be displaced by the sedimentation rate, since the test does not appear to be an index of activity except in a proportion of the larger and more serious lesions. This does not agree with the findings of Bannerman (48) who affirms that the test is a good index of the activity of a lesion. In smaller lesions no matter how active the focus is, the test seldom gives any indication of the process.

(c) RELATIONSHIP TO ABSCESS FORMATION.

Table 5.

Abscess	Sedimentation Rate (in minutes)				
	300	200-299	100-199	-100	Total
In Minor Lesion	2	6	-	-	8
In Major "	1	2	11	22	36
Total	3	8	11	22	44

The behaviour of the reaction in cases showing abscess formation is quite illuminating. In 8 minor lesions complicated by abscess all the readings were high, while in 36 lesions of major sort, similarly complicated, only 3 showed readings approaching normal; all others are definitely accelerated rates. Comparison with the line "not quiescent" of table 3 shows the possibility of some connection. Thus of 30 high or normal readings only 3 showed abscess formation, and/

and of 67 low readings 33 or rather less than half showed abscess formation. The fact that abscess formation is in the large majority of cases proof of activity, and the probability that all active disease is accompanied by abscess formation in some degree, as exemplified by Jones' (49) spindle shaped shadow in radiograms of the spine, and as suggested by Perkins (50) dealing with hip joint diseases, raise two points. The first has been touched on already when the rather wide scope of the term "not quiescent" was discussed. Possibly these cases are not active in the sense that progressive tissue disturbance is going on, but in spite of that they can by no means be labelled quiescent. The second based on the comparison of the lower readings of tables 3 and 5 raise the point as to whether or not the half of the active cases not having abscesses did not actually have some collection of debris. When it is said that only palpable or visible abscesses were taken on account of the possibility becomes more striking. The whole position while not mathematically clear cut is sufficiently definite to suggest the possibility of abscess formation in the presence of a low reading in an active case.

If such were the case one would be justified in expecting an increase in the sedimentation rate to give warning of the likelihood of the occurrence of abscess formation/

formation. In 6 major cases such a warning may be considered as having been given; in each a fall in the sedimentation rate preceded by a period up to six weeks after the discovery of the abscess. In all the fall was considerable, and in all the initial figure was reasonably high. In two other cases, a large abscess developed without any alteration in the blood sedimentation rate done specially to correlate the possible relationship between the two. In no case of disease of a major character was a rising sedimentation rate followed by abscess formation though such an occurrence took place in two minor lesions. Probably the rise in sedimentation rate is closely related to the presence of a collection of partially broken down albuminous material. Bannemman holds that a complication is foreshadowed by increase in the sedimentation rate. As far as concerns abscess in major lesions this investigation confirms his findings. In one case the treatment of a large abscess, the contents of which were of cheese like consistency, by fluid injections designed to produce liquifaction by leucocytosis was followed by a distinct acceleration in the rate, the lower figure remaining till the abscess dried up. Conversely in one boy with a large abscess which had been present a very considerable time and which could/

could not be emptied by needle, the reading steadily rose to a satisfactory figure. The abscess was cleaned out by open methods to remove his last bar to ambulant treatment, and at operation it was found to be partially calcified and very dry throughout.

(a) RELATIONSHIP TO SINUS FORMATION.

Throughout the whole series, 30 readings were coincident with the presence of sinuses, the age and condition of which varied from case to case. While the number is small the findings are given in tabular form on the same lines as for abscess formation. Again those cases dealt with under amyloid disease are excluded.

Table 6.

Sinus	Sedimentation Rate (in minutes)				Total
	300	200-299	100-199	-100	
In Major Lesion	5	1	7	6	19
In Minor Lesion	3	2	6	-	11
Total.	8	3	13	6	30

The outstanding features of the table are few. No minor lesion with sinuses gave a reading of less than 100 minutes, where as six cases of major disease were so recorded. In the zone of medium readings the findings offer no/

no definite information, in that as many major as minor lesions showed this type of reading; and at first sight a very similar state prevails among the high and normal figures. It so happened that among the 6 normal readings in line 1, are included four, taken from a man who had excision of the knee done 18 months before, but who had still one small unhealed area in the scar. The knee itself was firmly ankylosed. At the extreme opposite end of the table, among the low minor readings, three readings must be specially mentioned. These concern a case of tuberculous ankle with numerous sinuses, in whom the rate rose fairly steadily over rather more than 3 months. The foot was eventually amputated and the reading taken rather over one month later was normal. Probably this boy was in the preamyloid condition, where, as mentioned before, the rate becomes progressively faster.

With these allowances it might be stated that widely speaking sinuses as such have little bearing on the rate. The factor concerned is again the lesion causing the sinuses, the smaller lesion having little influence on the blood conditions except after persisting a very considerable period. Of some importance too is the nature of the sinuses: Readings, as would be/

be expected, are low where the sinus is the result of the recent break down of a large abscess, in which case the rate is probably as much a sign of very active progressive disease as anything. Conversely, the reading is likely to be high where a sinus is the result of the retention of a minute sequestrum as in the case previously cited. Finally there is the gradual merging from simple sinus formation through a range of falling readings to a condition of amyloid degeneration. This has been dealt with already.

(d) IN PARAPLEGIA.

No conclusions can be reached on any relationship there may be between the sedimentation rate and paraplegia. Only three cases with cord interference came into the investigation and paraplegia of itself seemed to have no effect on the rate. Two of the cases were paraplegics with inactive though not yet consolidated spines and both had high readings throughout. Both are now rather over a year after the first reading alive and fully recovered. The third was a paraplegia in an elderly man with a very active spine. Readings in his case were never over 100 minutes and he has since died.

IN DIAGNOSIS.

No/

No non-tuberculous cases were dealt with among the bone and joint group and accordingly no findings under this head can be offered.

IN PROGRESS AND TREATMENT.

Table 7.

Lesion	Sedimentation Rate.			Total	
	Improved (or slower)	Worse (or faster)	Stationary or variable.		
Improved	13	2	10	25	See Note 1.
Worse	—	2	2	4	See Note 2.
Stationary	1	3	2	6	See Note 3.
Total	14	7	14	35	

Above is given a synopsis of the condition of the patients at the end of the investigation and any change there may have been in the sedimentation rates. Only those patients having two or more readings are included and only major lesions.

Note 1. Of 25 patients whose lesions were thought to have improved during the period under observation, the sedimentation rate improved in 13. In 10 others the rate showed little change, but all these had very good normal readings at the commencement. Two cases showed improvement

of/

of the lesion, but poorer sedimentation rate. One of these has now, about one year later, a definite pulmonary lesion. The other can in no way be explained,

Note 2. Here correspondence is absolute. Two patients showed lesions becoming progressively worse and a coincident increase in the blood sedimentation rate. Other two who likewise became worse showed a fairly speedy rate, but both commenced at a very low figure. One of them has now definite amyloid disease.

Note 3. One patient showed little change in the local lesion but his sedimentation rate became less rapid, though not greatly so. One year later he has still active disease but is in good general health. Three showed no improvement in the lesion, and the rate became more rapid. One of these has since died of meningitis and one has developed another major bone lesion with abscess formation. Two cases showed maintenance of comparable levels clinically and serologically.

On the whole the correspondence between rise and fall in the blood sedimentation rate and improvement and degeneration of the lesion is close. Again it seems as in pulmonary tuberculosis improvement clinically marches with a slowing of the rate, but it must be noted that if the test is to be of value the original reading and changes in the rate from that are of more importance than

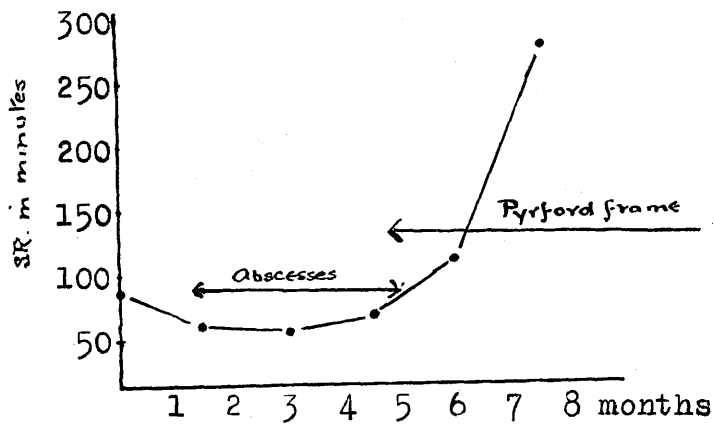
any/

any conclusion drawn from a single estimation. Among minor lesions the test offers no information, except perhaps in the developement of new lesions. Only four cases of minor disease had two or more readings and are not tabulated.

Little need be said of treatment apart from progress. Reference has already been made to the increasing rate as amyloid degeneration becomes established and as the less fluid collections of debris become sufficiently liquid to allow of aspiration. The change in the rate as abscesses become dry can only be in part put down to aspiration, and part to treatment on general lines. Two outstanding features might be added. In two cases of abscess with a high rate, this rate improved when sinus formation allowed of adequate drainage. Thereafter the sedimentation rate changed according as to whether the sinuses cleared up, as in one case, when the rate improved, or persisted as they did in the other. One practical finding seems to have been the increased rate following forcible manipulation of hips showing bad deformity. In almost all cases so treated the sedimentation rate increased, in most only temporarily. In some, however, it was accompanied by clinical activity. Accordingly the method of dealing with such cases has been altered, and the common practice now/

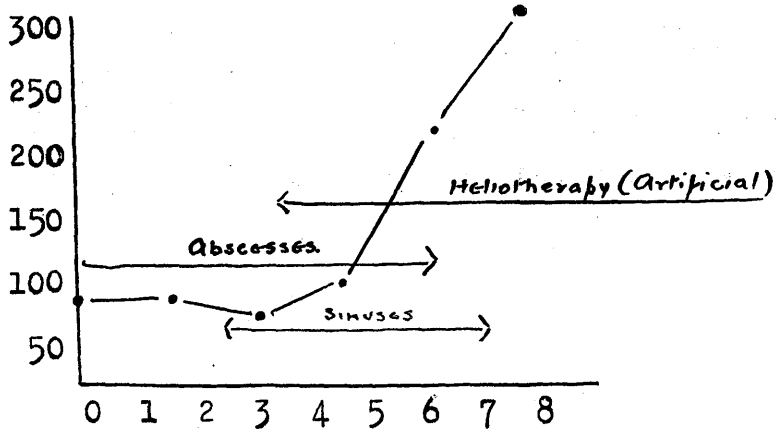
now is to perform subtrochanteric osteotomy. In certain patients, heliotherapy was found to have an extremely good effect, and in many this change was definitely reflected in an improved sedimentation rate. Following a graph of a routine case treated by appliances and aspiration, is a graph of a case similarly treated but with artificial heliotherapy added.

Graph 1.



J.H. (graph 1) had very acute hip joint disease with considerable deformity. He later, at a point between the 1st and 2nd months of treatment developed two abscesses, one in Scarpas triangle, and one in the right iliac fossa. These were aspirated till his 5th month of treatment when he was put on a Pyrford frame. Thereafter he improved rapidly, and his abscesses have not recurred.

Graph 2.



A.K. (graph 2) A very acute knee with several abscesses, and general condition poor as a result of severe toxaemia. Temperature very irregular till almost 4½ months after admission. Fresh abscesses developed between 2nd and 3rd month of treatment and his original abscesses had given place to sinuses. Routine treatment was given till between the 3rd and 4th month when small but increasing exposures to ultra-violet light from a 25 amp. Tungsten-Carbon arc were added. Thereafter he steadily improved and has now been inactive for over six months, and up in a plaster case.

IN COMPLICATION.

Apart from the common complications arising in course of treatment of bone and joint tuberculosis, such as abscess formation and development of sinuses, paraplegia or recrudescence of activity, the only outstanding features were as follows.

(a) The development of or recrudescence of a pulmonary lesion/

lesion. In several patients known to have pulmonary disease, it was found that over all the readings were lower than the average and the rate fell more slowly during the course of treatment. In one case the change was marked. This boy's spine became inactive and consolidated and the reading was satisfactory. Ambulant treatment in a plaster jacket then commenced, seems to have lit up or brought to light a hitherto unsuspected pulmonary focus and his reading some time later dropped to a much lower figure, the rate being increased roughly 50%. The value of the test in this and comparable cases, was however, slight as the ward chart was, shortly after getting up, strongly suggestive of such a development.

(b) In the development of new lesions: In only one case of a major lesion did a fresh major lesion develop . When this was recognised the sedimentation rate was done, and his already low figure was greatly reduced. The great reduction may be explained by the fact that both lesions went on to abscess formation. In another case of what appeared to be a minor lesion, the reading over 3 months was inexplicably low. This boy is now a definite example of multiple tuberculosis. In all other minor lesions developing one or at most two fresh minor lesions the rate remained unaltered.

In/

In view of these cases it seems probable that a low reading must be very fully explored before being disregarded, as it would seem to be significant of the onset of a large fresh lesion or of numerous other foci not all necessarily small.

IN PROGNOSIS.

The table following is built on the initial readings of the 50 bone and joint lesions and is strictly analogous to Table 10 in the section on pulmonary tuberculosis.

Table 8.

Initial reading (in mins)	No.	Deaths	Losing ground	Condition as at last reading.	Fit and progressing.
50 & below	3	1	1	—	1
51 - 100	9	1	2	4	2
101 - 200	12	2	3	1	6
201 - 250	6	-	1	1	4
250	21	-	-	6	15
Total	51	4	7	12	28

Briefly reviewed the table is not so striking as the corresponding details in the matter of pulmonary tuberculosis. The number of deaths is not so high, but as in the pulmonary table No.10 it is noticeable that all of them are associated with very fast rates at the first reading.

Arguing/

Arguing on similar lines it must be remarked that no patient with an initial normal reading has died or has been reported as losing ground; on the contrary of the 21 cases so tabulated 15 are known to be fit, and the remaining 6 are still having active treatment. This represents a higher proportion than offered by any other line of the table. Results closely approaching this are found in the 201-250 minute group, a group which is only slightly subnormal. Similarly working upwards towards the faster rates, it is seen that in the time which has elapsed between the investigation and the time of the patients' reporting, a progressive smaller proportion attain fitness or even equilibrium as the sedimentation rate becomes faster.

The case marked X has already been mentioned. He was re-admitted apparently arrested but convalescent after scarlet fever.

Summing up one realises that unlike the test on pulmonary tuberculosis a low rate need not mean a definitely bad prognosis. That death in this investigation was associated with the faster rates is significant but not conclusive since it has already been shown that a low rate may be associated with abscess formation. On one point there can be little doubt, and that is that those fortunate enough/

enough to be admitted with a good figure attain arrestment and fitness in a shorter time than those with fast rates.

THE TEST IN ABDOMINAL TUBERCULOSIS.

Only 5 patients involving 8 readings are available for review in this paragraph. As was previously remarked, this group of patients furnished the lowest average reading of all the non-pulmonary cases, and at the same time the lowest-highest reading (see table 2). The suggestive feature of a summary of the readings is that the case soonest dismissed was a boy whose lesion was apparently a simple tabes mesenterica, and who furnished the highest reading of all - 279 minutes to the 18 mm. mark. The next highest reading (111 minutes) was that of a boy suffering from a tuberculous plastic peritonitis. He made no improvement, was taken home before a second reading was got, and has since died. Lower still as a first reading is one of 83 minutes. This a pure tabes mesenterica was very quickly convalescent and is now well. The remaining two patients with readings of 57 and 40 minutes respectively both showed a tuberculous peritonitis with noticeable free fluid in the peritoneal cavity. It is significant that neither of these has done well. One is still a patient, now progressing slowly but steadily; the other was summarily discharged for disciplinary reason/

reasons and was not well at that time.

No conclusions of any unimpeachable value can be drawn from the above cases. The coincidence of low readings, free peritoneal fluid and slow progress is obvious, but further proof of a definite connection would be necessary.

THE TEST IN GENITOURINARY TUBERCULOSIS

Through insufficiency of cases a strictly comparable state of affairs exists among genitourinary lesions. Four patients were tested giving 12 readings. Two had bilateral inoperable renal disease and epididymitis and the figures show wide discrepancies. One case alone showed constitutional symptoms and here the sedimentation rate starting at 146 minutes became faster to the end. Throughout the urine was T.B.++. Two similar cases without constitutional symptoms, one with negative urine and prostatic involvement and one with kidney, and that proved to be involved, and urine T.B.++ showed high readings. The former in spite of his prostatic involvement is well and active. The other, unfortunately, cannot be traced. The fourth case was one of bilateral epididymitis. Throughout he showed good normal figures which did not alter after operation. He remains well. In two, the train of events is obviously suggestive, but until further investigation/

investigation, the results are inconclusive.

THE TEST IN LUPUS AND ADENTIS.

Five patients were tested. Throughout the 7 readings taken there was not the slightest evidence that the lesions had any effect on the sedimentation rate. The lowest reading (216 minutes) was got in a case of cervical adentis with chronic sinus formation. This has since healed completely.

SUMMARY AND APPLICATIONS.

(1) The average speed in non-plumonary tuberculosis is slower than in tubercle of the lung.

(2) The test cannot displace clinical and radiological examination as a test of activity except as qualified in summary No.3. below.

(3) High speeds seem to be definitely associated with abscess formation in major lesion. Accordingly a high sedimentation rate is the more suggestive of activity, and careful examination for abscess is necessary before such a reading is discarded as fallacious. A slow rate is not an accurate negative guide in this respect.

(4) Small persistent sinuses do not affect the rate. In major lesions with chronic sinuses, a persistent rapid rate over several readings suggests the onset of amyloid degeneration and should definitely raise the question of radical operative/

operative interference.

(5) The test appears to be unrelated to paraplegia apart from the cause thereof.

(6) A slowing sedimentation rate is the usual concomitant of clinical progress, and the test in many instances reflects the effect of certain lines of treatment.

(7) An increasingly rapid sedimentation rate in the absence of abscess formation may denote the recrudescence or development of a pulmonary or other new lesion. A seemingly minor lesion and a high falling speed may be the only evidence of early multiple foci.

(8) The test is of considerable prognostic value, but it is not so high as in pulmonary disease.

(9) In abdominal, genitourinary, and skin and gland tuberculosis, the results are inconclusive.

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